Remarks

Claims 1-27, 32, 36, 37, 69 and 77 are pending. Claims 28-31, 39, and 70-74 stand withdrawn. Reconsideration is requested in view of the above changes and the following remarks.

Claim 36 is amended to include only breast, prostate, lung, and colorectal cancers.

Response to 112 Rejection, and Objection to Claim 36

Claim 36 stands rejected under 35 U.S.C. 112, first paragraph as not enabling for diseases other than breast cancer, prostate cancer, lung cancer, and colorectal cancer. While Applicants disagree with the rejection, in an effort to advance prosecution, Claim 36 has been amended to recite treatment of breast, prostate, lung, and colorectal cancers. Furthermore, the term "colorectal skin" was objected to. The present amendment deletes the term "skin." Thus, claim 36 is believed to be in condition for allowance.

Response to 103 Rejection

Claims 1-3 were rejected under 35 U.S.C. 103(a) as unpatentable over Schwan et al., J. Org. Chem, **1998**, 63(22) 7825-2832 ("Schwan et al."). In the Office action on p. 4, the Examiner alleges that "Applicants claimed the [*sic*] compound of the general formula 1 differs from the teaching of the prior art references in that the instantly claimed compound of the general formula 1 is a homolog of the prior art compounds." Applicants strongly disagree that a methyl substitution on ring B as claimed is "homologous" to the teachings of Schwan et al.. First, the term homolog, or "homologous series" applies only to differences in the number of methylene (CH_2) groups in an alkyl chain, i.e. carbon atoms. Homologs are not described by compounds in which hydrogen on an aryl group is replaced by carbon, but rather a homolog is a compound in which a CH_2 group is inserted into a pre-existing carbon chain or alkyl group. In order to clarify this point, Applicants provide entries for the term "homologous series" from two chemical dictionaries in an Appendix (*Hawley's Condensed Chemical Dictionary, 13th Ed.*, Van Nostrand Reinhold, New York, 1997; *Glossary of Chemical Terms, 2nd Ed.*, Van Nostrand Reinhold, New York, 1982). Schwan et al. does not have such an alkyl group on phenyl, but

teaches only unsubstituted phenyl groups, i.e. phenyl groups having only hydrogen substituents at every substitutable position. In contrast, ring B of the claimed invention must have at least one non-hydrogen substituent. Applicants have already amended the claims to exclude unsubstituted phenyl groups. Schwan et al. does not teach or suggest the addition of a carbon-containing group such as methyl as a substituent on the phenyl ring, nor would Schwan et al. suggest to one of ordinary skill to make the substitution or modification to prepare the claimed compounds.

Furthermore, the Examiner directed the applicants to *In re Henze*, 181 F.2d 196, 85 USPQ 261 (C.C.P.A. 1950). Incidentally, *In re Henze* adopts the same definition for "homologous series" as discussed above. *In re Henze*, 181 F.2d 196 at 200. *In re Henze* addresses only homologs in which the compared compounds differ in number of carbons in the same alkyl chain, which cannot apply to the difference between Schwan et al. and the claimed invention, as discussed above. *In re Henze* does not address the differences between an alkyl substitution and a hydrogen substitution, for example. Therefore, *In re Henze* does not support the asserted obviousness rejection.

The Examiner directed the applicants to *In re Wood*, 582 F.2d 638, 199 USPQ 137 (C.C.P.A. 1978). In *In re Wood*, the claimed compounds were 7,7-dimethyl-7,8-dihydropteridines, while the cited prior art taught unsubstituted 7,8-dihydropteridines. In agreeing with the PTO that the prior art rendered the claimed compounds *prima facie* obvious, the court relied not only on the structural similarity between them, but also on the prior art's recognition that the unsubstituted pteridines had the same antimicrobial properties as the claimed compounds. *In re Wood*, 582 F.2d 638 at 641. Applicants respectfully point out that the pteridines of *In re Wood* are not aromatic, as in the instant claims, and further that the claimed compounds of *In re Wood* were designed to block aromaticity by virtue of gem 7,7-dialkyl substitution in the saturated ring. *In re Wood*, 582 F.2d 638 at 641. The instant claimed compounds include a substituted aromatic ring. Schwan et al. does not demonstrate any therapeutic utility or advantage for any of the disclosed compounds, and Schwan et al. lacks a

teaching of alkyl substituted phenyl as claimed. Thus *In re Wood* does not support the instant obviousness rejection.

The Examiner directed the applicants to *In re Wertheim*, 541 F.2d 257, 191 USPQ 90 (C.C.P.A. 1976). Applicants have found no relevance of this case, since *In re Wertheim* is directed to overlapping ranges. Therefore, *In re Wertheim* does not support the asserted obviousness rejection.

Finally, not only does Schwan et al. lack a teaching of alkyl substituted phenyl as claimed, but Schwan et al. does not teach or suggest the desirability of making such a substitution, nor does Schwan et al. demonstrate any therapeutic utility or advantage for any of the disclosed compounds. On these bases, a skilled practitioner would not have been motivated to practice the teachings of Schwan et al. to arrive at the instantly claimed compounds, as alleged by the Examiner on p. 4 of the Office action. Applicants refer the Examiner to *Eisai Co. Ltd. V. Dr. Reddy's Laboratories Ltd.,* 87 USPQ2d 1452, 1457 (Fed. Cir. 2008) ("post-*KSR*, a prima facie case of obviousness for a chemical compound still, in general, begins with the reasoned identification of a lead compound."). Schwan et al. does not provide a motivation to make a change, such as any substitution to the phenyl ring, because the reference does not teach a therapeutic utility for any lead compound. More specifically, Schwan et al. does not provide a motivation to make a particular carbon-containing substitution on the phenyl ring, as claimed. *See Eisai*, 87 USPQ2d at 1356 ("*KSR* presupposes that the record up to the time of invention would give some reasons, available within the knowledge of one of skill in the art, to make particular modifications to achieve the claimed compound. *See Takeda* 492 F.3d at 1357 ("Thus, in cases involving new chemical compounds, it remains necessary to identify some reason that would have led a chemist to modify a known compound in a particular manner to establish prima facie obviousness of a new claimed compound.").") (emphases added). The foregoing passage cites *Takeda Chem. Indus. v. Alphapharm Pty., Ltd.,* 492 F.3d 1350, 83 USPQ.2d 1169 (Fed. Cir. 2007). Since the Examiner has not established a prima facie case of obviousness, the rejection should be removed.

Response to Double Patenting Rejection

Claims 1-27, 32, 36-37, 69 and 77 were provisionally rejected under the judicially created doctrine of obviousness-type double patenting as unpatentable over claims 1-6, 8, 94-95, 97-117, 122, 128 and 130-132 of co-pending U.S. Application No. 10/592,604. Without acquiescing in the rejection, applicant notes that the rejection is provisional, since the allegedly conflicting claims in the '604 application have not been patented.

For the convenience of the Examiner, the following is the status of the '604 application. In the '604 application, a Restriction Requirement was issued on March 5, 2008. On April 2, 2008, Applicants elected Group 1, with traverse. In the Office Action mailed June 9, 2008, the Examiner vacated the Election/Restriction in favor of a new restriction/Lack of Unity. In a telephone conversation with Applicants' representative on June 4, 2008, Applicants provisionally elected Group 1 with traverse. Since the instant application is the earlier-filed application, no response is required at this time. MPEP 1490.V.D.

Request for Rejoinder of Claims 28-31, 39 and 70-74

Claims 28-31 and 39 are directed to conjugates of compounds of allowable claim 1 (claims 28-30), pharmaceutical compositions thereof (claim 31) and methods of treating breast, prostate, lung and colorectal cancer by administration of those conjugates (claim 39). These claims are directed to non-elected inventions that depend from or otherwise require all the limitations of an allowable claim to an elected invention, namely claim 1.

Accordingly, rejoinder and allowance of claims 28-31 is requested pursuant to MPEP 821.04(a):

> Rejoinder Between Product Inventions; Rejoinder Between Process Inventions.
>
> When restriction was required between independent or distinct products, or between independent and distinct processes, and all claims directed to an elected invention are allowable, any restriction requirement between the elected invention and any nonelected invention that depends form or otherwise requires all the limitations of an allowable claim should be withdrawn."

For the same reason, rejoinder and allowance of claim 39 is requested pursuant to MPEP 821.04(b):

> Rejoinder of Process Requiring an Allowable Product.
>
> Where claims directed to a product and to a process of making and/or using the product are presented in the same application, applicant may be called upon under 35 U.S.C. 121 to elect claims to either the product or a process. See MPEP § 806.05(f) and § 806.05(h). The claims to the nonelected invention will be withdrawn from further consideration under 37 CFR 1.142. See MPEP § 821 through § 821.03. However, if applicant elects a claim(s) directed to a product which is subsequently found allowable, withdrawn process claims which depend from or otherwise require all the limitations of an allowable product claim will be considered for rejoinder. All claims directed to a nonelected process invention must depend from or otherwise require all the limitations of an allowable product claim for that process invention to be rejoined. Upon rejoinder of claims directed to a previously nonelected process invention, the restriction requirement between the elected product and rejoined process(es) will be withdrawn.

Claims 70 and 71 depend from claim 69. The only basis for rejection of claim 69 (which depends from allowable claim 3) has been overcome, as discussed above. Claim 69 is therefore allowable. Rejoinder an allowance of claims 70 and 71 is requested, since claims 70 and 71 depend from claim 69. The basis of rejoinder is MPEP 821.04(b), reproduced above.

Claims 72 and 73 are directed to a process of making a compound of allowable claim 2. Claims 72 and 73 are thus rejoinable pursuant to MPEP 821.04(b).

Claim 74 is a process for making compounds of certain sulfones compounds of Formula V. The scope of Formula V has been amended to reduce the scope of n to n=1. The process utilizes, as a starting material, a compound according to Formula I. The scope of the compound of Formula I, as defined in claim 74, is identical to the scope of the compound of Formula I set forth in allowable claim 1. Claim 74 is thus rejoinable pursuant to MPEP 821.04(b) as process claims which requires all the limitations of an allowable product claim.

Conclusion

Applicants respectfully submit that the application is in good and proper form for allowance, and the Examiner is respectfully requested to pass this application to issue. If, in the

opinion of the Examiner, another telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned attorney.

Respectfully submitted,

E. PREMKUMAR REDDY, *et al.*

BY _____

DANIEL A. MONACO
Registration No. 30,480
Drinker Biddle & Reath LLP
One Logan Square
18th and Cherry Streets
Philadelphia, PA 19103-6996
Tel: (215) 988-3312
Fax: (215) 988-2757
Attorney for Applicants

CH01/ 25213665.2